Paper No. 40

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KAARE M. GAUTVIK, PETER ALESTROM, TORDIS B. OYEN and ODD S. GABRIELSEN

Appeal No. 2001-1974
Application No. 08/340,664

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 31-35, which are all the claims pending in the application.

Claims 31 and 33 are illustrative of the subject matter on appeal and are reproduced below:

31. hPTH (1-84), as a substantially homogeneous protein.

33. hPTH (1-84), as a substantially homogeneous protein, prepared by a process comprising the steps of:

providing a microorganism containing exogenous DNA encoding hPTH (1-84);

culturing said microorganism to allow expression of said exogenous DNA, thereby producing hPTH (1-84); and

purifying said hPTH (1-84) as a substantially homogenous protein.

The references relied upon by the examiner are:

Brewer (Brewer)	3,888,132	May 7, 1995
Mayer (Mayer)	EP 0,139,076	May 2, 1985
Kaisha et al. (Kaisha)	GB 2,092,596 A	Aug. 18,1982

Breyel et al. (Breyel), "Synthesis of Mature Human Parathyroid Hormone in Escherichia coli," Third European Congress on Biotechnology, Vol. III, pp. 363-69 (1984)

Sung et al. (Sung), "Hybrid Gene Synthesis: its application to the assembly of DNA sequences encoding the human parathyroid hormones and analogues," Biochem. Cell Bio., Vol. 63, pp. 133-38 (1986)

GROUNDS OF REJECTION

Claims 33-35 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claims 31 and 32 stand rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under U.S.C. 103 as obvious over Brewer.

Claims 31-34 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Breyel, Sung, or Mayer, in view of Kaisha.

We affirm the rejection of claims 31 and 32 under 35 U.S.C. § 102(b) as being anticipated by Brewer. Accordingly, we do not reach the alternative rejection of claims 31 and 32 under 35 U.S.C. § 103 as being unpatentable over Brewer. We reverse the rejection of claims 33-35 under 35 U.S.C. § 112, second paragraph. We reverse the rejection of claims 31-34 under 35 U.S.C. § 103 as being unpatentable over either Breyel or Sung in view of Kaisha. We vacate the rejection of claims 31-34 under 35 U.S.C. § 103 over Mayer in view of

Kaisha. In addition, we identify other issues for the consideration of both the examiner and appellants.

CLAIM GROUPING

Appellants set forth two groupings of claims: (I) claims 31 and 32; and (II) claims 33-35. Brief, page 5. According to appellants the claims in each claim group stand or fall together. Id. Accordingly, we limit our discussion to representative independent claims 31 and 33. Claim 32 will stand or fall together with claim 31, and claims 34 and 35 will stand or fall together with claim 33. 37 CFR § 1.192(c)(7) (1998).

DISCUSSION

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

The examiner finds (Answer, page 4), "[t]he claims as they are currently written contain no reference to the secretory leader sequence and recite only expression of hPTH[ ](1-84), which is not described by the specification as originally filed." According to the examiner (id.), "[t]he omission of the sequence encoding the secretory leader amounts to a gap between the elements of the DNA to be expressed in the method recited in the claim, which is a product by process type claim."

We see no requirement in claims 33-35 that hPTH be secreted from the microorganism. Claim 33 simply requires hPTH be produced followed by the purification of hPTH as a substantially homogeneous protein. Claims 34 and 35 merely identify the microorganism as E. coli (claim 34) or yeast (claim 35). In addition, we cannot agree that the specification as "originally filed" contains no

reference to hPTH (1-84) as recited in appellants' claims. To the contrary, the specification discloses (page 5) that mature hPTH is an 84 amino acid protein. Furthermore, page 3 of the specification discloses, "it is an object of the present invention to provide a plasmid for insertion in yeast containing DNA coding for parathyroid hormone." As set forth in Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991):

> The statute requires that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." A decision as to whether a claim is invalid under this provision requires a determination whether those skilled in the art would understand what is claimed. See Shatterproof Glass Corp. v. Libbey-Owens Ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir. 1985) (Claims must "reasonably apprise those skilled in the art" as to their scope and be "as precise as the subject matter permits.").

Furthermore, claim language must be analyzed "not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary skill in the pertinent art." In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971). In this regard, we recognize appellants' argument (Brief, page 6) that the specification discloses, "a variety of leader sequences can be employed in the recombinant production of hPTH according to the invention. See page 5, lines 6-10, of the [a]pplication."

For the foregoing reasons, we disagree with the examiner that the claims contain a missing element and are therefore indefinite. Accordingly, we reverse the rejection of claims 33-35 under 35 U.S.C. § 112, second paragraph.

REJECTION UNDER 35 U.S.C. § 102(b)/103:

Claim 31 stands rejected under 35 U.S.C § 102(b) as anticipated by or, in the alternative, under 35 U.S.C § 103 as being obvious over Brewer. To support this rejection, the examiner finds (Answer, page 5), Brewer "disclose highly purified human PTH." According to the examiner (id.), Brewer's "preparation was pure enough to sequence 34 amino acid residues starting at the amino terminus of the protein. Thus, the protein as purified by Brewer et al. appears to be consistent with the limitations of the instant claims with respect to being 'substantially homogeneous' hPTH. Correlating Brewer to appellants' specification, the examiner finds (id.),

> the only portion of the specification which relates to purity is the disclosure that the protein was partially sequenced (page 7, starting at line 27), which the ordinary artisan would recognize as requiring a relatively pure preparation of the desired protein.... Based upon the fact that the specification discloses obtaining the sequence of 19 and 45 amino acids respectively, from the yeast and E. coli-produced protein, Brewer's ability to obtain 34 amino acids would seem to indicate that comparable purity was achieved.

In response, appellants note (Brief, page 7), "[h]omogeneity is not needed for sequencing." While this may be true, claim 31 is not drawn to a homogenous protein. Instead, claim 31 is drawn to a "substantially homogenous" protein. Since, homogenous would refer to a pure preparation, it is unclear from the specification what degree of purity is intended by "substantially" homogenous. We are unable to identify, and appellants do not refer to, a portion of appellants' specification that defines the term "substantially homogenous." Therefore, to the

extent that Brewer's purification protocol results in impure material[1], appellants have not established on this record that the impure material of claim 31 is different from that disclosed by Brewer.

We are not persuaded by appellants' argument that the hPTH sequence disclosed by Brewer contains errors. In this regard, we agree with the examiner (Answer, page 8) that appellants' claims are not limited to any particular sequence, and when read in light of the specification (e.g. page 15) may include non-native human sequences. We are also not persuaded by appellants' arguments (Brief, pages 8-9) regarding biological activity of hPTH, since claim 31 does not require the substantially homogeneous protein to be biologically active. See Answer, page 10.

To the extent that appellants argue (Brief, page 8) that Brewer does not disclose an intact protein, we note that Brewer disclose (column 1, lines 19-22), "[t]he complete amino acid sequence of the 84 amino acid parathyroid hormone from the bovine and porcine species have been reported." Brewer further disclose (column 2, lines 50-54), "[t]he purified human parathyroid hormone migrated as a single component on disc gel electrophoresis with a mobility which was identical to that of the bovine parathyroid hormone." This migration pattern suggests that Brewer's purified human parathyroid hormone is 84 amino acids in length.

Anticipation under 35 U.S.C. § 102 requires that a single prior art reference disclose each and every limitation of the claimed invention. Electro

[1] See appellants arguments (Brief, page 7) and paragraph 9 of the Maggio Declaration.

Med. Sys. S.A. v. Cooper Life Sci., 34 F.3d 1048, 1052, 32 USPQ2d 1017, 1019 (Fed. Cir. 1994). In our opinion the examiner has provided the evidence necessary to establish that Brewer discloses a substantially homogeneous hPTH (1-84) protein. Accordingly, we affirm the rejection of claim 31 under 35 U.S.C. § 102(b) as anticipated by Brewer. Having found that Brewer anticipates claim 31, we do not address the alternative rejection of claim 31 under 35 U.S.C. § 103. As set forth above, claim 32 falls together with claim 31.

REJECTION UNDER 35 U.S.C. § 103:

Claims 31-34 are rejected under 35 U.S.C. § 103 as being unpatentable over any one of Breyel, Sung, or Mayer in view of Kaisha.

Breyer or Sung in view of Kaisha:

According to the examiner (Answer, page 6) each of Breyel, Sung and Mayer teach the expression of recombinant hPTH in bacteria, but do not purify the protein from the bacterial cell extracts. The examiner relies on Kaisha to make up for this deficiency in Breyel, Sung and Mayer. According to the examiner (Answer, bridging paragraph, pages 6-7), Kaisha teaches that hPTH can be easily obtained by conventional purification and separation teachniques.

In response appellants argue (Brief, page 10) that Breyel teaches that PTH has a short half-life in E. coli, "[t]hus, from the moment the hPTH is produced by E. coli in the method of Breyel et al., the hPTH composition will be contaminated by PTH fragments produced by the degradation of PTH." Accordingly, appellants conclude (id.), "Breyel et al. do not teach an intact and substantially homogeneous hPTH protein, as claimed by [a]pplicants."

Regarding Sung, appellants argue (id.), "Sung et al. did not produce recombinant hPTH protein, instead they constructed a plasmid having the sequence for hPTH(1-84), and suggest that they are conducting a study of the expression of these gene products." In addition, appellants note (Brief, bridging paragraph, pages 10-11) that since Sung inserted the plasmids in an E. coli expression system they would be expected to have a short half-life as taught by Breyel. Accordingly, appellants conclude (Brief, page 11), "Sung et al. do not teach or suggest [a]pplicants' claimed invention."

Appellants' arguments (Brief, page 12) limit Kaisha to the purification of hPTH from human lymphoblastoid cells, which according to appellants are "barely contaminated with host animal cells." We are not persuaded by this argument. The fact that lymphoblastoid cells would be "barely contaminated with host animal cells" would be equally true for a pure culture of any cell, e.g. the bacteria taught by Breyel and Sung. Nevertheless, we are persuaded by appellants' arguments concerning Breyel and Sung.

According to the examiner (Answer, page 12), "[i]t would have been within the skill of the ordinary artisan to have separated the full-length (1-84) [hPTH protein] from the degraded forms of the product, to obtain the claimed homogeneous preparation." According to the examiner (id.), given the teachings of Kaisha, a "person of ordinary skill in the art would be able to devise a protocol for purifying such [a degraded preparation of protein] with a reasonable expectation of success and without undue experimentation...." However, we find nothing in Kaisha to support this position, and the examiner offers no additional

evidence to support her position that it would be within the skill of the art as taught by Kaisha to purify intact hPTH (1-84) from a degraded preparation protein with a reasonable expectation of success. As appellants argue, there is no suggestion in either of Breyel or Sung that any intact protein could be obtained. Based on the evidence of record, it is our opinion that, at best, it would have been obvious to try to isolate "intact protein" from the degraded preparations of Breyel and Sung. "Obvious-to-try," however, is not the standard of obviousness under 35 U.S.C. § 103. See In re O'Farrell, 858 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). Accordingly, we reverse the rejection of claims 31-34 under 35 U.S.C. § 103 as being unpatentable over either Breyel, or Sung, in view of Kaisha.

Mayer in view of Kaisha:

This rejection stands on a different footing. The Mayer document relied upon by the examiner is in the German language. This record does not reflect that the examiner considered an English language translation of this foreign language document. We recognize with appreciation that appellants included a copy of the English language abstract for this document. However, the evidentiary basis for this rejection is the full text of this document, and it stands to reason that full text documents will provide more facts. Since obviousness determinations are fact-intensive, it is not apparent why the examiner and appellants have satisfied themselves with determining patentability under 35 U.S.C. § 103 on less than a complete factual record.

As set forth in Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1033 (Fed. Cir. 1997), "For an appellate court to fulfill its role of judicial review it must have a clear understanding of the grounds for the decision being reviewed," which requires that "[n]ecessary findings must be expressed with sufficient particularity to enable [the] court without resort to speculation, to understand the reasoning of the board, and to determine whether it applied the law correctly and whether the evidence supported the underlying and ultimate fact-findings." Like the Court of Appeals in Gechter, this board requires a clear understanding of the grounds for the decision being reviewed. In this case, we find it difficult to understand the examiner's reasoning and whether the evidence upon which he relies supports the underlying fact-findings for the rejections under 35 U.S.C. § 103. The board cannot examine in the first instance all applications which come before it in an ex parte appeal under 35 U.S.C. § 134. In this particular appeal, we have elected not to expend board resources to obtain the needed translation. Accordingly, we vacate the rejection of claims 31-34 under 35 U.S.C. § 103 as being unpatentable over Mayer in view of Kaisha, and remand the application to the examiner for further consideration. Upon return of the application, the examiner should obtain an English language translation of the Mayer document. If upon review of this document, the examiner remains of the opinion that the claims on appeal are unpatentable, she should issue an appropriate Office Action that sets forth the facts and reasons used in support of such a rejection.

OTHER ISSUES

Product-by-process:

We note that claims 33-35 are drafted in product-by-process format. Similar to claim 31, claims 33-35 require only that the protein preparation be "substantially homogeneous." Therefore, absent evidence to the contrary, a reference that anticipates, or renders obvious claim 31, would also anticipate, or render obvious claims 33-35. We remind the examiner and appellants that the determination of patentability in product-by-process claims is based on product itself, even though such claims are limited and defined by a process. In re Thorpe, 777 F.2d 695, 697, 227 USPQ 964, 966 (Fed. Cir. 1985). "[W]here a product-by-process claim is rejected over a prior art product that appears to be identical, although produced by a different process, the burden is upon the applicants to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 710 F.2d 799, 803, 218 USPQ 289, 292-93 (Fed. Cir. 1983).

Accordingly, we encourage the examiner to take a step back and reconsider claims 33-35 together with the available prior art. If after this review the examiner finds that the claims on appeal are unpatentable, she should issue an appropriate Office Action that sets forth the facts and reasons used in support of such a rejection.

Standard:

We note that appellants' specification teaches (e.g., page 7) the use of an "hPTH standard(1-84)" to compare and assess the results of the purification process. The specification teaches that the purification product eluted in the same peak as this standard and comigrated with the standard as one band on a gel. The specification implicitly asserts that these comparisons demonstrate the purity and completeness of the protein being claimed. Upon return of the application, the examiner and appellants should work together to determine whether this "standard" is available prior art against claims 31-35.

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FURTHER PROCEEDINGS

We are not authorizing a Supplemental Examiner's Answer under the provisions of 37 CFR § 1.193(b)(1). Any further communication from the examiner that contains a rejection of the claims should provide appellants with a full and fair opportunity to respond.

TIME PERIOD FOR RESPONSE

In addition to affirming the examiner's rejection of one or more claims, this decision contains a remand to the examiner. Therefore, in order to preserve appellants' right to seek review under 35 U.S.C. § 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If further prosecution before the examiner does not result in allowance of the application, abandonment or a second appeal, this case should be returned

to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing hereof.

No time period for taking subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; VACATED and REMANDED

Sherman D. Winters)
Administrative Patent Judge)
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Toni R. Scheiner) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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